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SURVEY OF BRIARANE-TYPE DITERPENOIDS – PART IV

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Abstract – The structures, names, bioactivities, and references of 90 briarane-type diterpenoids, including 59 new compounds, are described in this review. All the briarane-type compounds mentioned in this review article were obtained from various octocorals including *Briareum*, *Dichotella*, *Ellisella*, *Junceella*, *Menella*, *Verrucella,* and *Ptilosarcus*. Some of these compounds showed potential bioactivities.

1. INTRODUCTION

This review is of the literature from Sep. 2008 to Feb. 2011 and describes 90 briarane-type diterpenoids (including 59 new compounds), which possess a bicyclo[8.4.0] carbon skeleton and most possess a

γ-lactone moiety in structures (Figure 1). As in previous reviews,[1–3] we showed the structures, names, bioactivities, and references for these briaranes. Most briarane derivatives mentioned in this article were isolated from the octocorals belonging to the order Gorgonacea, including *Briareum excavatum*, *Briareum* sp., *Dichotella gemmacea*, *Ellisella robusta*, *Junceella fragilis*, *Junceella juncea, Menella* sp., and *Verrucella* sp.; and the order Pennatulacea, including *Ptilosarcus gurneyi*. The first iodine-containing briaranes, dichotellides A–E, were found in a gorgonian *Dichotella gemmacea*.[4] This survey of briarane-type compounds will be presented taxonomically according to genus and species.

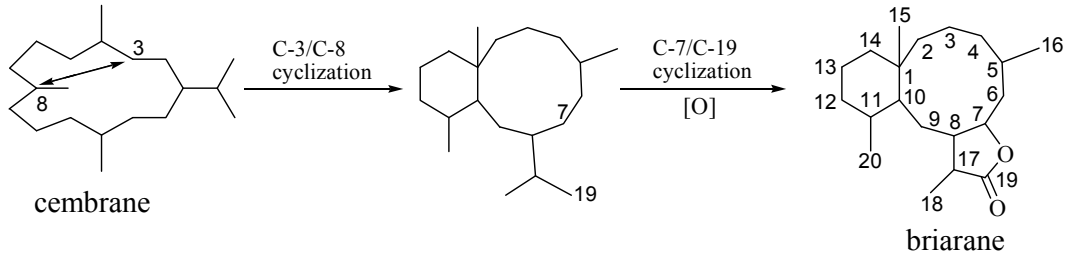


Figure 1. Possible biogenetic origin of briarane-type metabolites. The numbering system shown is those presently in use.

2. GORGONACEA

2.1. *Briareum* (family Briareidae)

A. *Briareum excavatum*

The gorgonian corals belonging to the genus *Briareum* played a main role to produce the briarane-type natural products. In the continuing studies on the Formosan octocorals, the gorgonian *B. excavatum* (including cultured type and field type), was further studied for their complex and interesting chemical constituents. 27 briarane derivatives, including 26 new compounds, briaexcavatins Q–Z (**1**–**10**),[5–7] excavatoids A–P (**11**–**26**),[8–12] and a known metabolite, briaexcavatin I (**27**),[8,13] were isolated from *Briareum excavatum* (Table 1). The structures of new briaranes **1**–**26** were determined by spectroscopic methods and the structures for briaexcavatins U (**5**), W (**7**), and excavatoid A (**11**) were further confirmed by single-crystal X-ray diffraction analyses.[6–8] The absolute configuration of **5** was also determined directly by its X-ray structure.[6] The X-ray structure for the known briarane, briaexcavatin I (**27**), was reported for the first time.[8] Briaranes **1**–**12** and **15**–**27** were isolated from a cultured type *B. excavatum*.[5–12]

Among the above compounds, briaexcavatin Y (**9**) is the first briarane containing a C-8/9 epoxy group.[7] Excavatoid A (**11**) is the first briarane possessesing six hydroxy groups and a 17-methoxy group.[8] Excavatoid C (**13**) is the first 12,13-secobriarane possessing a novel pentacyclic skeleton with an ε-lactone.[8] Excavatoid P (**26**) is the only briarane known to possess a 6β-chlorine atom.[12] The relationships between ^{13}C NMR chemical shifts and the conformations of briaranes possessing an 11,12-epoxy group are also described.[7] The 11,12-epoxide was assigned as α configuration because the ^{13}C NMR chemical shifts for these two carbons were $\delta_C < 60$ ppm (δ_C 57–60 ppm); while the chiral carbons C-11 and C-12 existed in *S**

and *R** form, respectively, and leading the epoxy group to α-orientation. If the epoxy group was found to exist in β-configuration (11*R** and 12*S**), the ^{13}C chemical shifts for C-11 were shifted downfield and appeared at δ_C 61–66 ppm, and most chemical shifts for C-12 in these briaranes were $\delta_C > 60$ ppm.[7] It is noteworthy to note that the natural briaranes possessing an 11,12-epoxy group in β form were all isolated from the octocorals distributed in the West Pacific Ocean.[7]

In the biological activity testing, briaexcavatin S (**3**) and excavatoids H–J (**18**–**20**) exhibited weak cytotoxicity toward various tumor cells.[5,10] Briaexcavatins V (**6**), X (**8**), Y (**9**),[7] and excavatoids D–F (**14**–**16**),[8,9] L–P (**22**–**26**),[11,12] showed various inhibitory effects on superoxide anion generation or elastase release by human neutrophils at 10 μg/mL. Briaexcavatin Z (**10**) was not active in inhibition of superoxide anion generation but this compound exhibited mild activity to enhance human neutrophil elastase release at 10 μg/mL.[7]

Table 1. The Briarane-Type Metabolites from *B. excavatum*

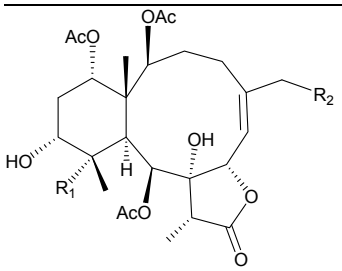
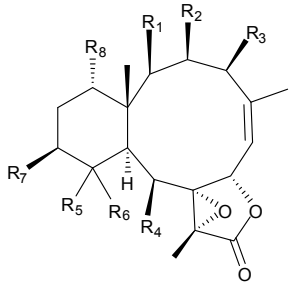
Structure	No.	Name	Biological activity	Ref.
	**1**	briaexcavatin Q (R_1 = OH, R_2 = Cl)	n.r.[a]	5
	10	briaexcavatin Z (R_1 = R_2 = H)	not active in inhibition of superoxide anion generation (0.7%) but exhibited mild activity to enhance human neutrophil elastase release (inhibition rate –29.0%) at 10 μg/mL	7
	**2**	briaexcavatin R (R_1 = R_4 = R_8 = OAc, R_2 = H, R_3 = R_7 = OH, R_5 = α-H, R_6 = β-methyl)	n.r.	5
	3	briaexcavatin S (R_1 = R_3 = R_8 = OAc, R_2 = H, R_4 = R_7 = OH, R_5 = α-OH, R_6 = β-methyl)	IC_{50} (CCRF-CEM) = 37.8 μg/mL	5
	16	excavatoid F (R_1 = R_4 = R_7 = R_8 = OAc, R_2 = R_3 = H, R_5 = β-OH, R_6 = α-methyl)	showed an inhibitory effect on elastase release (30.6%), but not active in inhibition of superoxide anion generation (2.6%) at 10 μg/mL	9
	17	excavatoid G (R_1 = R_7 = R_8 = OAc, R_2 = R_3 = H, R_4 = OH, R_5 = β-OH, R_6 = α-methyl)	not active in cytotoxicity testing with CCRF-CEM, HL-60, DLD-1, and IMR-32 cells (IC_{50} > 40 μg/mL)[a]	10
	20	excavatoid J (R_1 = R_4 = R_8 = OAc, R_2 = H, R_3 = $OC(O)(CH_2)_2CH_3$, R_5 = α-OH, R_6 = β-methyl, R_7 = OH)	IC_{50} (CCRF-CEM, HL-60, DLD-1, IMR-32) = > 40.0, 38.4, 25.1, > 40.0 μg/mL	10
	21	excavatoid K (R_1 = R_2 = R_4 = R_7 = R_8 = OH, R_3 = H, R_5 = α-H, R_6 = β-methyl)	not active in cytotoxicity testing with CCRF-CEM, HL-60, DLD-1, and IMR-32 cells (IC_{50} > 40 μg/mL)	10
	22	excavatoid L (R_1 = R_4 = R_8 = OAc, R_2 = R_7 = OH, R_3 = H, R_5 = α-H, R_6 = β-methyl)	showed inhibitory effects on superoxide anion generation (42.4%) and elastase release (31.3%) at 10 μg/mL	11

Table 1. The Briarane-Type Metabolites from *B. excavatum*

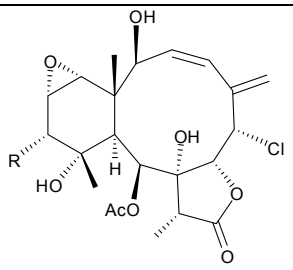
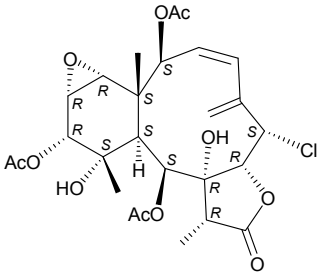
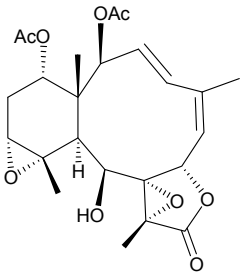
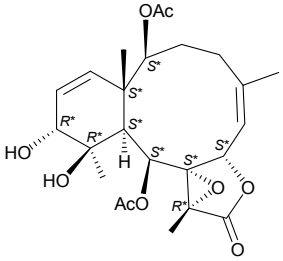
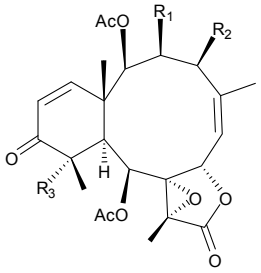
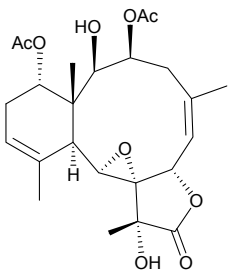
Structure	No.	Name	Biological activity	Ref.
	**4**	briaexcavatin T (R = $OC(O)(CH_2)_2CH_3$)	n.r.	5
	**5**	briaexcavatin U	not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells (IC_{50} > 50 μg/mL)	6
	**6**	briaexcavatin V	showed weak inhibitory effects on superoxide anion generation (11.4%) and elastase release (23.3%) at 10 μg/mL	7
	**7**	briaexcavatin W	not active in inhibition of superoxide anion generation (4.2%) and elastase release (–0.6%) at 10 μg/mL	7
	**8**	briaexcavatin X (R_1 = H, R_2 = R_3 = OH)	showed a weak inhibitory effect on superoxide anion generation (13.7%), but not active in inhibition of elastase release (3.2%) at 10 μg/mL	7
	18	excavatoid H (R_1 = $OC(O)(CH_2)_2CH_3$, R_2 = R_3 = H)	IC_{50} (CCRF-CEM, HL-60, DLD-1, IMR-32) = 13.1, > 40.0, 21.4, > 40.0 μg/mL	10
	**9**	briaexcavatin Y	showed a weak inhibitory effect on superoxide anion generation (17.5%), but not active in inhibition of elastase release (1.6%) at 10 μg/mL	7

Table 1. The Briarane-Type Metabolites from *B. excavatum*

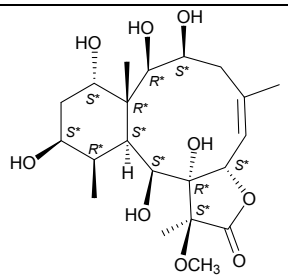
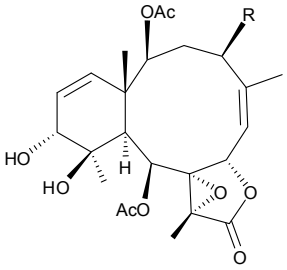
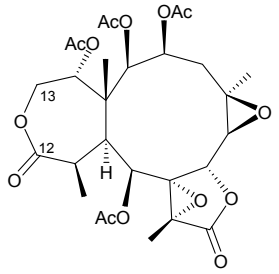
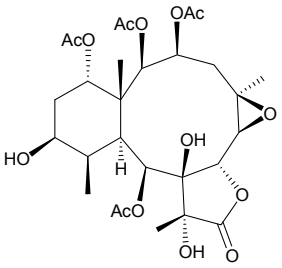
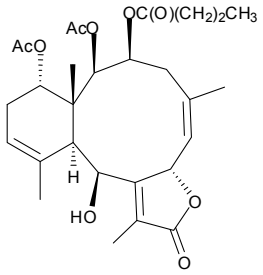
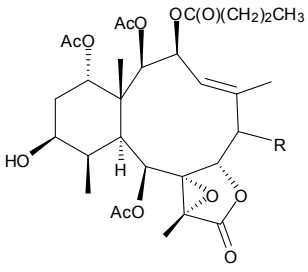
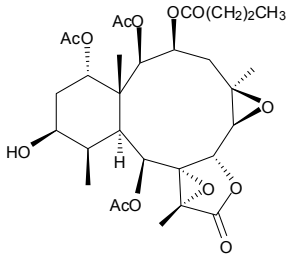
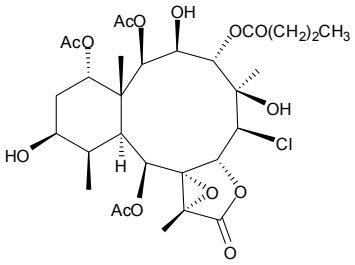
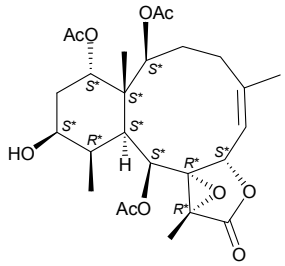
Structure	No.	Name	Biological activity	Ref.
	**11**	excavatoid A	not active in inhibition of superoxide anion generation and elastase release at 10 μg/mL not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells	8
	**12**	excavatoid B (R = $OC(O)(CH_2)_2CH_3$)	not active in inhibition of superoxide anion generation and elastase release at 10 μg/mL not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells	8
	19	excavatoid I (R = OAc)	IC_{50} (CCRF-CEM, HL-60, DLD-1, IMR-32) = > 40.0, > 40.0, > 40.0, 31.1 μg/mL	10
	**13**	excavatoid C	not active in inhibition of superoxide anion generation and elastase release at 10 μg/mL not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells	8
	**14**	excavatoid D	showed inhibitory effects on superoxide anion generation (23.8%) and elastase release (39.4%) at 10 μg/mL not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells	8
	**15**	excavatoid E	showed weak inhibitory effects on superoxide anion generation (13.0%) and elastase release (26.2%) at 10 μg/mL	9
	**23**	excavatoid M (R = α-OH)	showed weak inhibitory effects on superoxide anion generation (14.9%) and elastase release (17.0%) at 10 μg/mL	11
	24	excavatoid N (R = β-OH)	showed weak inhibitory effects on superoxide anion generation (10.9%) and elastase release (22.2%) at 10 μg/mL	11

Table 1. The Briarane-Type Metabolites from *B. excavatum*

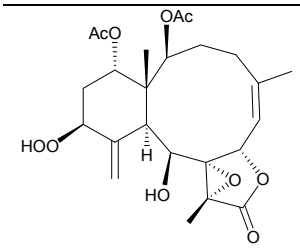
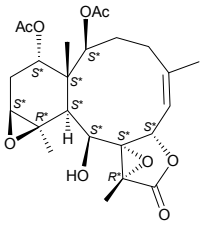
Structure	No.	Name	Biological activity	Ref.
	**25**	excavatoid O	showed a weak inhibitory effect on elastase release (16.9%) at 10 μg/mL	12
	**26**	excavatoid P	showed a weak inhibitory effect on elastase release (16.1%) at 10 μg/mL	12
	**27**	briaexcavatin I	not active in inhibition of superoxide anion generation (2.4%) at 10 μg/mL	8,13

[a]n.r. = not reported. [b]CCRF-CEM (human T-cell acute lymphoblastic leukemia), HL-60 (human promyelocytic leukemia), DLD-1 (human colon adenocarcinoma), and IMR-32 (human neuroblastoma).

B. *Briareum* sp.

In continuing studies on the chemical constituents of a gorgonian coral identified as *Briareum* sp., collected from a tank equipped with a flow-through water system, located in the National Museum of Marine Biology and Aquarium, Taiwan, a new hydroperoxybriarane, briarenolide D (**28**), and a known briarane, 2β-acetoxy-2-(debutyryloxy)stecholide E (**29**), were obtained (Table 2).[14,15] The structure of hydroperoxybriarane **28** was established by spectroscopic methods and the structure of **29** was confirmed by a single-crystal X-ray diffraction analysis for the first time.[14] In previous studies, only two hydroperoxybriaranes, brianthein B and briarenolide B, were isolated from the gorgonian corals *Briareum excavatum* and *Briareum* sp., collected off Indonesian and Taiwan waters, respectively.[16,17] Briarenolide D (**28**) is the third briarane possessesing a hydroperoxy group. It is interesting to note that the methylenecyclohexane ring in **28** was found to possess a twist boat conformation by the interpretation of proton chemical shifts and NOESY correlations analyses.[14,18] The natural products of this type (hydroperoxybriarane) could be a chemical marker for the gorgonian corals belonging to the genus *Briareum*. Briarenolide D (**28**) exhibited moderate cytotoxicity toward DLD-1 and CCRF-CEM cells.[14]

Table 2. The Briarane-Type Metabolites from *Briareum* sp.

Structure	No.	Name	Biological activity	Ref.
	**28**	briarenolide D	IC_{50} (DLD-1, CCRF-CEM, HL-60, P-388D1) = 9.6, 6.9, > 40, > 40.0 μg/mL[a]	14
	**29**	2β-acetoxy-2-(debutyryloxy)stecholide E[b]		14,15

[a]P388D1 (murine macrophage cell). [b]The cytotoxic data of briarane **29** had been reported, please see ref. 15.

2.2. *Dichotella* (family Ellisellidae)

A. *Dichotella gemmacea*

The gorgonian corals belonging to the family Ellisellidae also played major sources of briarane-type natural products.[1–3] The South China Sea gorgonian coral *D. gemmacea* was found to contain nine chlorinated briarane-related natural products, including five new compounds, dichotellides A–E (**30**–**34**) (Table 3),[4] and four known briaranes, praelolide, juncin P, juncin ZI, junceellin A.[19] The structures of new briaranes **30**–**34** were established by spectroscopic methods, and the absolute stereochemistry of dichotellide A (**30**) was further confirmed by a single-crystal X-ray diffraction analysis.[4] Dichotellides A–E (**30**–**34**) are the first examples of iodine-containing briarane-type natural products.[4] Dichotellide C (**32**) showed marginal cytotoxicity toward SW1990 cells.[4]

Table 3. The Briarane-Type Metabolites from *D. gemmacea*

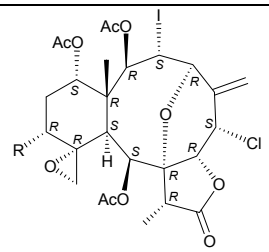
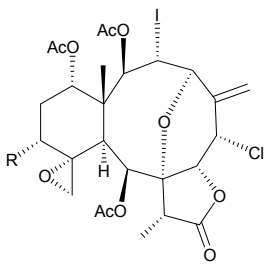
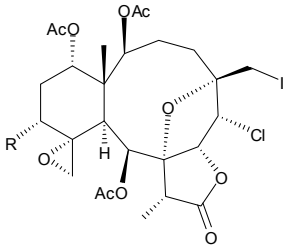
Structure	No.	Name	Biological activity	Ref.
	**30**	dichotellide A (R = $OC(O)CH_2CH(CH_3)_2$)	not active in cytotoxicity testing with MCF-7, SW1990, HepG2, and H460 cells[a]	4
	**31**	dichotellide B (R = OAc)	not active in cytotoxicity testing with MCF-7, SW1990, HepG2, and H460 cells[a]	4
	32	dichotellide C (R = H)	showed marginal cytotoxicity against SW1990 cells (IC_{50} = 45.0 μM), but not active toward MCF-7, HepG2, and H460 cells	4

Table 3. The Briarane-Type Metabolites from *D. gemmacea*

Structure	No.	Name	Biological activity	Ref.
	**33**	dichotellide D (R = $OC(O)CH_2CH(CH_3)_2$)	not active in cytotoxicity testing with MCF-7, SW1990, HepG2, and H460 cells	4
	34	dichotellide E (R = OAc)	not active in cytotoxicity testing with MCF-7, SW1990, HepG2, and H460 cells	4

[a]MCF7 (human breast carcinoma), SW1990 (human pancreatic adenocarcinoma), HepG2 (human hepatocellular carcinoma), H460 (large cell lung cancer).

2.3. *Ellisella* (family Ellisellidae)

A. *Ellisella robusta*

Five chlorinated briaranes, including four new compounds, robustolides J–L (**35**–**37**) and 12-*epi*-fragilide G (**38**),[5,20,21] along with a known compound, robustolide H (**39**),[20,22] were further isolated from a Formosan gorgonian coral *E. robusta* (Table 4). The structures of new briaranes **35**–**38** were established by spectral data analysis. Both the six-membered rings in briaranes **35** and **37** were found to exist in twist boat conformation.[5,20] The X-ray structure, including the absolute stereochemistry, for the known briarane, robustolide H (**39**), was also reported for the first time.[20] The structure for a known briarane, juncin F,[23] which was first isolated from a gorgonian coral *Junceella juncea*, collected off the Red Sea, was further established by comparison of the proton chemical shifts and coupling patterns with those of robustolide H (**39**).[5]

Robustolides J–L (**35**–**37**) and 12-*epi*-fragilide F (**38**) showed inhibitory effects on superoxide anion or elastase release by human neutrophils and robustolide L (**37**) exhibited weak cytotoxicity toward IMR-32 cells.[5,20,21]

Table 4. The Briarane-Type Metabolites from *E. robusta*

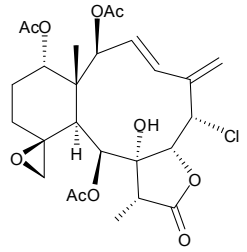
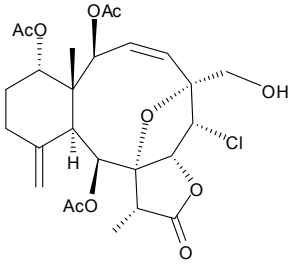
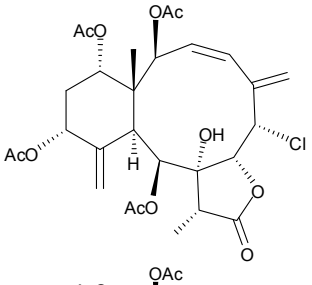
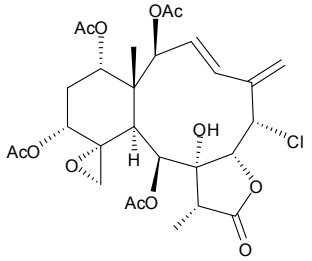
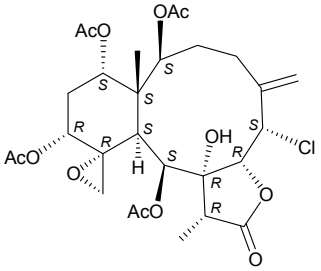
Structure	No.	Name	Biological activity	Ref.
	**35**	robustolide J	showed an inhibitory effect on superoxide anion generation (IC_{50} = 5.4 μg/mL)	5
	**36**	robustolide K	showed an inhibitory effect on superoxide anion generation (IC_{50} = 6.4 μg/mL)	5

Table 4. The Briarane-Type Metabolites from *E. robusta*

Structure	No.	Name	Biological activity	Ref.
	**37**	robustolide L	showed a weak inhibitory effect on superoxide anion generation (13.9%) at 10 μg/mL IC_{50} (IMR-32) = 33.8 μg/mL	20
	**38**	12-*epi*-fragilide G	showed an inhibitory effect on elastase release (61.4 %) at 10 μg/mL	21
	**39**	robustolide H	n.r.	20,22

2.4. *Junceella* (family Ellisellidae)

A. *Junceella fragilis*

Study on the gorgonian coral *J. fragilis*, collected off the Southern Taiwan coast, has afforded six new briarane derivatives, fragilides E–J (**40**–**45**) (Table 5-1),[18,20,24,25] along with three known compounds, junceellonoid D, juncin Z, and (+)-11β,20β-epoxyjunceellolide D.[26,27] The structures of new briaranes **40**–**45** were established by spectroscopic methods. The absolute configuration of fragilide F (**41**) was determined by its X-ray structure.[18] Fragilide I (**44**) is the first briarane possessing a 9-isovaleroxy group.[25] Fragilides E (**40**) and J (**45**) displayed weak inhibitory effects on elastase release by human neutrophils,[20,24] and juncin Z exhibited significant cytotoxicity towad CCRF-CEM cells (IC_{50} = 1.6 μg/mL).[18]

Table 5-1. The Briarane-Type Metabolites from *J. fragilis*

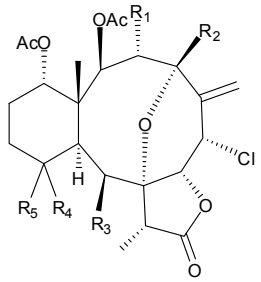
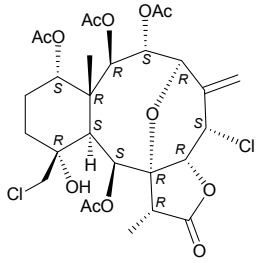
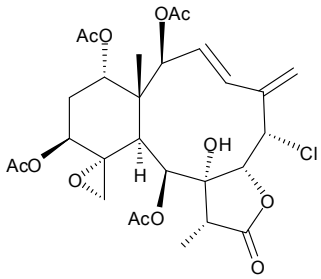
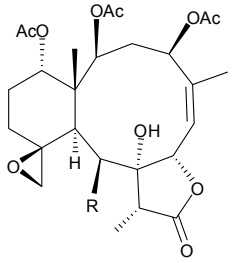
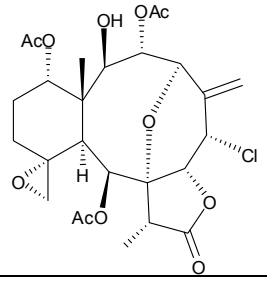
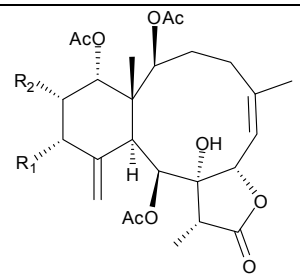
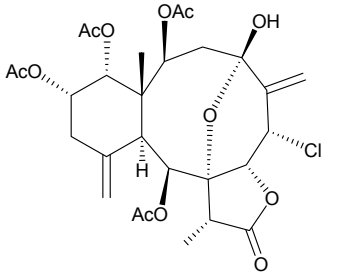
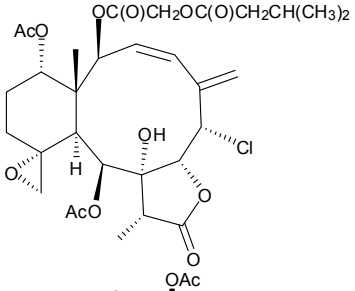
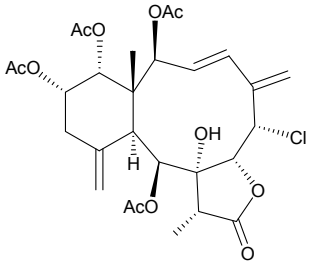
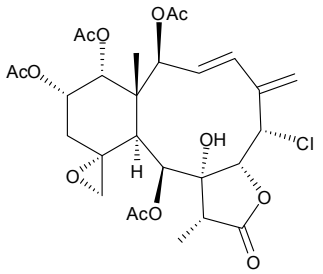
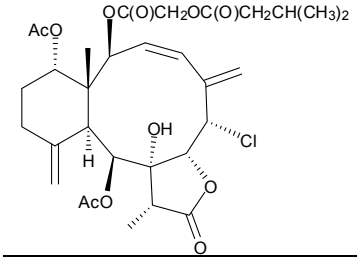
Structure	No.	Name	Biological activity	Ref.
	**40**	fragilide E (R_1 = OAc, R_2 = H, R_3 = OH, R_4 = β-OH, R_5 = α-CH_2OAc)	showed weak inhibitory effects on superoxide anion generation (16.6%) and elastase release (17.7%) at 10 μg/mL	24
	43	fragilide H (R_1 = H, R_2 = OH, R_3 = OAc, R_4 = α-OH, R_5 = β-CH_2Cl)	not active in cytotoxicity testing with DLD-1, CCRF-CEM, HL-60, and P388D1 cells (IC_{50} > 40 μg/mL)	25

Table 5-1. The Briarane-Type Metabolites from *J. fragilis*

Structure	No.	Name	Biological activity	Ref.
	**41**	fragilide F	not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells (IC_{50} > 40 μg/mL)	18
	**42**	fragilide G	not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells (IC_{50} > 40 μg/mL)	18
	**44**	fragilide I (R = $OC(O)CH_2CH(CH_3)_2$)	not active in cytotoxicity testing with DLD-1, CCRF-CEM, and P388D1 cells (IC_{50} > 40 μg/mL)	25
	**45**	fragilide J	showed a weak inhibitory effect on elastase release (11.5%) at 10 μg/mL	20

In addition, seven new briaranes, frajunolides E–K (**46**–**52**) (Table 5-2),[28] and 14 known briaranes, praelolide, junceellin, junceellolides A–E and K, (–)-11β,20β-epoxy-4-deacetoxyjunceellolide D,[27] umbraculolide A, junceellonoid A, and juncins Y, Z, ZI,[29] were isolated from the gorgonian coral *J. fragilis*, collected in Taitong County, Taiwan. The structures of new briaranes **46**–**52** were established by spectroscopic methods. It has to be noted that the structure of briarane **48** (frajunolide G) had been reported in a previous study and named as fragilide D.[30] Frajunolides E (**46**), F (**47**), I (**50**), and J (**51**) exhibited weak inhibitory effects on superoxide anion generation or elastase release by human neutrophils.[28] Based on the characteristics of chemical shifts for the briarane derivatives contained a C-11/20 carbon-carbon double bond, the chemical shifts for the olefin protons H_2-20 were summed up; these appear at δ_H 4.95–5.30 ppm and δ_H 4.85–5.15 ppm, while the cyclohexane rings to show a twist boat conformation. Furthermore, the proton NMR data for H_2-20 appeared at δ_H 4.95–5.10 ppm and δ_H 4.40–4.75 ppm, the cyclohexane rings were found to exist in a chair conformation.[18]

Table 5-2. The Briarane-Type Metabolites from *J. fragilis*

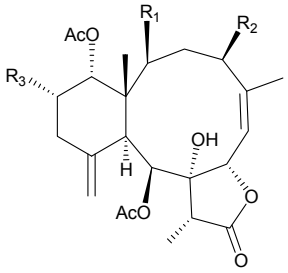
Structure	No.	Name	Biological activity	Ref.
	**46**	frajunolide E (R_1 = H, R_2 = OAc)	showed weak inhibitory effects on superoxide anion generation (17.5%) and elastase release (27.4%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)[a]	28
	51	frajunolide J (R_1 = OC(O)Et, R_2 = H)	showed weak inhibitory effects on superoxide anion generation (20.1%) and elastase release (19.9%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)	28
	**47**	frajunolide F	showed a weak inhibitory effect on elastase release (10.4%), but not active in inhibition of superoxide anion generation (7.4%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)	28
	**48**	frajunolide G (= fragilide D)	not active in inhibition of superoxide anion generation (–7.5%) and elastase release (8.3%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)	28,30
	**49**	frajunolide H	not active in inhibition of superoxide anion generation (–1.9%) and elastase release (0.1%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)	28
	**50**	frajunolide I	showed a weak inhibitory effect on elastase release (18.2%), but not active in inhibition of superoxide anion generation (–10.3%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)	28
	**52**	frajunolide K	not active in inhibition of superoxide anion generation (2.4%) and elastase release (8.0%) at 10 μg/mL not active in cytotoxicity testing with Hep2, Doay, WiDr, and Hela cells (IC_{50} > 20 μg/mL)	28

[a]Hep2 (human liver carcinoma), Doay (human medulloblastoma), WiDr (human colon adenocarcinoma), Hela (cervical epitheloid carcinoma).

B. *Junceella juncea*

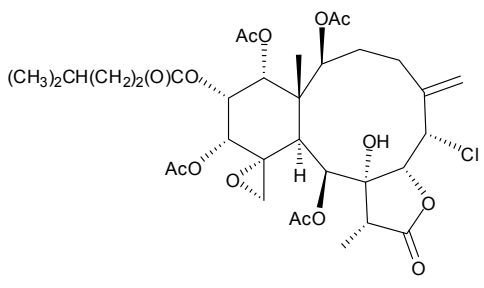
Fvie new 8-hydroxybriaranes, junceols D–H (**53**–**57**) (Table 6-1), were isolated from a Formosan gorgonian coral *Junceella juncea*.[31] The structures of briaranes **53**–**57** were determined on the basis of spectroscopic methods and the methylenecyclohexane rings in **53**–**57** were found to exist in twist boat form. Junceols D (**53**) and F–H (**55**–**57**) exhibited cytotoxicity toward CCRF-CEM or DLD-1 cells and junceols E–H (**54**–**57**) displayed weak inhibitory effects on superoxide anion generation by human neutrophils at 10 μg/mL.[31]

Table 6-1. The Briarane-Type Metabolites from *J. juncea*

Structure	No.	Name	Biological activity	Ref.
	**53**	junceol D (R_1 = $OC(O)CH(CH_3)_2$, R_2 = $OC(O)CH_2CH(CH_3)_2$, R_3 = OAc)	not active in inhibition of superoxide anion generation (6.0%) at 10 μg/mL IC_{50} (CCRF-CEM, DLD-1) = 1.3, 1.0 μg/mL	31
	54	junceol E (R_1 = $OC(O)CH(CH_3)_2$, R_2 = OAc, R_3 = H)	showed a weak inhibitory effect on superoxide anion generation (25.6%) at 10 μg/mL IC_{50} (CCRF-CEM, DLD-1) = > 40.0, > 40.0 μg/mL	31
	55	junceol F (R_1 = $OC(O)CH(CH_3)CH_2CH_3$, R_2 = OAc, R_3 = H)	showed a weak inhibitory effect on superoxide anion generation (23.5%) at 10 μg/mL IC_{50} (CCRF-CEM, DLD-1) = 4.9, > 40.0 μg/mL	31
	56	junceol G (R_1 = $OC(O)CH(CH_3)CH_2CH_3$, R_2 = H, R_3 = OAc)	showed a weak inhibitory effect on superoxide anion generation (17.3%) at 10 μg/mL IC_{50} (CCRF-CEM, DLD-1) = 4.4, > 40.0 μg/mL	31
	57	junceol H (R_1 = OAc, R_2 = H, R_3 = $OC(O)CH(CH_3)_2$)	showed a weak inhibitory effect on superoxide anion generation (19.4%) at 10 μg/mL IC_{50} (CCRF-CEM, DLD-1) = 7.2, 17.0 μg/mL	31

In 2009, Qi et al., reported the occurrence of a new briarane derivative, juncin ZII (**58**) (Table 6-2),[32] along with three known metabolties, gemmacolides C, F, and (+)-11β,20β-epoxyjunceellolide D,[27,33] from a gorgonian coral *Junceella juncea*, collected at the South China Sea.[32] The structure of briarane **58** was established by spectroscopic method and this compound showed potential antifeedant and antifouling activity.[32] Moreover, a series of briarane derivatives, isolated previously from *J. juncea* by Qi's group were assayed for their potential antifeedant activity, cytotoxicity, and antifouling activity.[32,34,35]

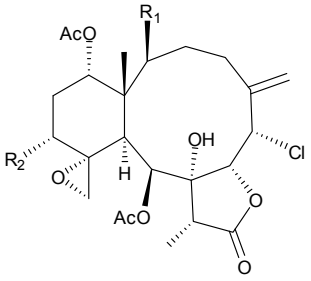
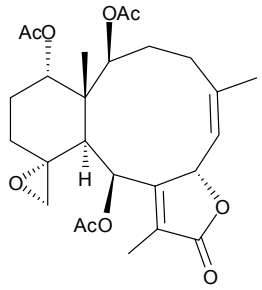
Table 6-2. The Briarane-Type Metabolite from *J. juncea*

Structure	No.	Name	Biological activity	Ref.
	**58**	juncin ZII	showed a medium antifeedant activity (84.5%) toward the second-instar larvae of *Spodoptera litura* at 500 μg/mL. showed a medium cytotoxicity (cell mortality: 20.5% in 24 h and 43.2% in 48 h) toward the second-instar larvae of *Spodoptera litura* at 100 μg/mL. showed an antifouling activity toward the barnacle *Balanus amphitrite* larvae at (EC_{50} = 0.004 μg/mL) not active in cytotoxicity testing with K562, A549, Hela, and Hep2 cells[a]	32

[a]K562 (human erythromyeloblastoid leukemia), A549 (human lung adenocarcinoma).

Chemical investigation on the gorgonian *J. juncea*, collected in the Taitong County, Taiwan, had yielded four new briaranes, juncenolides H–K (**59**–**62**) (Table 6-3).[36] The structures for briaranes **59**–**62** were determined on the basis of spectral data analysis.[36]

Table 6-3. The Briarane-Type Metabolites from *J. juncea*

Structure	No.	Name	Biological activity	Ref.
	**59**	juncenolide H (R_1 = R_2 = OAc)	showed weak inhibitory effects on superoxide anion generation (28.9%) and elastase release (15.1%) at 10 μg/mL	36
	60	juncenolide I (R_1 = $OC(O)CH(CH_3)_2$, R_2 = OAc)	showed a weak inhibitory effect on elastase release (15.6%), but not active in inhibition of superoxide anion generation (1.3%) at 10 μg/mL	36
	61	juncenolide J (R_1 = OAc, R_2 = $OC(O)CH(CH_3)_2$)	not active in inhibition of superoxide anion generation (–3.6%) and elastase release (2.1%) at 10 μg/mL	36
	**62**	juncenolide K	showed a weak inhibitory effect on elastase release (17.5%), but not active in inhibition of superoxide anion generation (–5.7%) at 10 μg/mL	36

2.5. ***Menella*** (family Ellisellidae)

A. ***Menella*** **sp.**

Two well known briaranes, junceellolides B and D, which were first isolated from the gorgonian coral *Junceella fragilis*,[37] were isolated from a gorgonian coral, identified as *Menella* sp., collected off Meishan Island, Hainan province, China.[38] Junceellolides B and D were the first two briarane-type natural products found in the gorgonian corals belonging to the genus *Menella*.[38]

2.6. ***Verrucella*** (family Ellisellidae)

A. ***Verrucella*** **sp.**

A well known chlorinated briarane, junceellin, which was first isolated from the gorgonian coral *Junceella squamata*,[39] was obtained from a gorgonian coral, identified as *Verrucella* sp., collected off the South China Sea.[40] Junceellin was the first briarane-type natural product found in the gorgonian corals belonging to the genus *Verrucella*.[40]

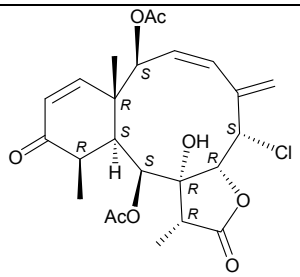
3. PENNATULACEA

3.1. Ptilosarcus (family Pennatulidae)

A. *Ptilosarcus gurneyi*

An insecticidal briarane, ptilosarcenone (**63**), which was first isolated from a North Pacific Ocean sea pen coral, *Ptilosarcus gurneyi*,[41,42] was obtained from the same species collected near Juneau, Alaska, 2006 (Table 7). The structure, including the absolute stereochemistry of ptilosarcenone was determined directly by a single-crystal X-ray study for the first time.[43]

Table 7. The Briarane-Type Metabolite from *P. gurneyi*

Structure	No.	Name	Biological activity	Ref.
	**63**	ptilosarcenone	toxic to the larvae of the tobacco hornworm *Manduca sexta* at 250 ppm	41,42,43

4. CONCLUSION

All the briarane-type compounds are proven to be marine origin, and up to date, over 500 new briarane-type natural diterpenoids had been isolated from various marine organisms, particularly with the soft corals belonging to the subclass Octocorallia. The structural novelty and interesting bioactivities of briarane derivatives are still prompted continuing attention. A series of semi-synthetic briarane derivatives are prepared from the well-known briaranes, such as briantheins X and Y, for their potential insecticidal activity.[44] The highly functionalized fragment corresponding to the Northern hemisphere of the briaranes also has been synthesized employing a series of organic reactions.[45] However, due to the structural complexity, it is difficult to synthesize the potential briaranes by chemical methods totally. Based on this point, we have to coordinate and make the best use of highly developed aquaculture technology to enhance in captivity mass production of raw material needed for extraction of marine natural product compounds such as briarane diterepnoids which also protect natural population and natural habits form over exploitation.

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National Sun Yat-sen University (98C0317020; and National Science and Technology Program for Biotechnology and Pharmaceuticals, National Science Council (NSC 99-2323-B-291-001 and NSC 98-2320-B-291-001-MY3), Taiwan, awarded to P.-J.S.

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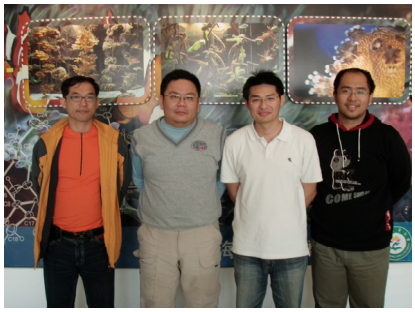

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